

AD_____

AWARD NUMBER: W81XWH-05-1-0321

TITLE: PROVIDER NEEDS FOR DISTRIBUTED SIMULATION EDUCATION
SYSTEM IN TOTAL INTRAVENOUS ANESTHESIA & TARGET CONTROLLED
INFUSION

PRINCIPAL INVESTIGATOR: W. BOSSEAU MURRAY, M.D.

CONTRACTING ORGANIZATION: PENNSYLVANIA STATE UNIVERISTY
HERSHEY, PA 17036

REPORT DATE: NOVEMBER 2008

TYPE OF REPORT: FINAL ADDENDUM

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 1 November 2008		2. REPORT TYPE Final Addendum		3. DATES COVERED 1 Mar 2005 – 31 Oct 2008	
4. TITLE AND SUBTITLE PROVIDER NEEDS FOR DISTRIBUTED SIMULATION EDUCATION SYSTEM IN TOTAL INTRAVENOUS ANESTHESIA & TARGET CONTROLLED INFUSION			5a. CONTRACT NUMBER		
			5b. GRANT NUMBER W81XWH-05-1-0321		
			5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) W. Bosseau Murray, M.D. E-Mail: wmurray1@hmc.psu.edu			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Pennsylvania State University Hershey, PA 17036			8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSOR/MONITOR'S ACRONYM(S)		
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Based on the military needs for a simpler anesthetic administration system with a smaller footprint, there is a desire in all the services to use TIVA. Compared with other current (inhalational) anesthesia modes, TIVA/TCI equipment is light-weight, easily transported by a single person, and operable without external (mains) power. This makes TIVA/TCI ideally suited to both military field operations and a wide range of hospital and clinic health care organizations. This concept was strongly supported by the PLR Committee at Long Beach, CA in Jan 2009. Total intravenous anesthesia (TIVA) via target controlled infusion (TCI) use is widespread outside the United States of America. However, TIVA and TCI is not yet widely used in the USA. Due to this unfamiliarity, the purpose of this project was to produce a TIVA training curriculum on an open web site. The scope of this project included selection of a minimum set of information needed, selection of a teaching philosophy and format, producing pharmaco-kinetic graphics of plasma concentrations using simulation programs, and finally, building and implementing a web site with linear and asynchronous (just-in-time) learning formats. We produced an open Web site " www.LearningTIVA.com " that enables trainees to follow either a linear learning path, a just-in-time path with clinical questions, and/or a step-by-step set of instructions to run three TIVA pharmaco-kinetic simulation programs. Following the creation of the website, the major findings based on the results from the feedback, indicated a high perceived value and benefit to clinicians learning about TIVA, using this type of learning modality. An accompanying Web Blog has been created for anonymous, safe (against hackers) feedback. The significance of the work is that a cadre of clinicians experienced in TIVA principles can now be developed. Applications for further funding has been submitted to TATRC (June 2009) and an Earmark (\$4.2 million) through the Office of Government Affairs of the Pennsylvania State University College of Medicine.					
15. SUBJECT TERMS Military Medicine, Anesthesia, Intravenous, Target controlled, Simulation, Education, Distance Education, web based education, TeleMedicine, TeleAnesthesia, computer based learning, clinical learning, residents, CRNA, CME, pharmacology, pharmacokinetics, target controlled anesthesia (TCI), total intravenous anesthesia (TIVA)					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	29	19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
A. Cover.....	1
B. SF 298.....	2
C. Table of Contents.....	4
D. Introduction.....	5
E. Body.....	6
F. Key Research Accomplishments.....	17
G. Reportable Outcomes.....	18
H. Conclusion.....	21
I. References.....	26
J. Appendices.....	27

D. Introduction

Developing a Web Site: Phase I extension for TIVA TCI

(Total Intra-Venous Anesthesia,
Target Controlled Anesthesia)

Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The **subject** of this project is TIVA (Total Intra-Venous Anesthesia) training via a website to enhance the safety of anesthesia for the war fighter. Based on the military needs for a simpler anesthetic administration system with a smaller footprint, there is a desire in all the services to use TIVA. However, TIVA is not yet widely used in the USA. Due to this unfamiliarity, the **purpose** of this project was to produce clinically relevant TIVA training on an open web site. The **scope** of this project included a needs assessment, selection of a minimum set of information needed, preparation of graphics of blood/plasma concentrations of propofol from pharmaco-kinetic simulation programs, selection of a teaching philosophy and format, and finally, building and implementation of a web site with linear and asynchronous (just-in-time) learning formats.

Footnote: Explanation of abbreviations and terms.

TIVA: Total intra-venous anesthesia implies all anesthetic agents being administered via the intra-venous route. This only requires a small, robust IV infusion device (small footprint, battery operated.) This is in contrast to inhalational anesthesia which typically requires a large and complex anesthesia machine with a much larger footprint.

TCI: target controlled infusion is commonly used in Europe. A computer controls the infusion pump, which uses a mathematical model to administer a very infusion rate to obtain a constant blood (plasma) level of each anesthetic agent.

TGI: target guided anesthesia can be accomplished via one of two methods:

- a. fixed (static) paper printouts (or fixed pages on a web site) which indicate generic infusions of say 3, 6, 9 and 12 hours of infusion at rates of say 133, 166, 200 and 250 ug/kg/min of propofol.
- b. a back bench computer into which is fed actual patient specific data (infusion rates) for a simulation program to calculate blood concentrations in real time. These calculations and predictions can be used as one of many sources of information for clinicians to make decisions about adjustments of the propofol infusion rates.

E. Body

E.1. Summary Abstract

Background:

Total intravenous anesthesia (TIVA) via target controlled infusion (TCI) use is widespread outside the United States of America. The use of TIVA/TCI in patient care provides excellent anesthesia with minimal over or under-use of anesthetic agents, providing an excellent, safe patient experience and cost effective health care (pharmacy, equipment, and provider team utilization). In addition, compared with other current anesthesia modes, TIVA/TCI equipment is light-weight, easily transported by a single person, and operable without external power. This makes TIVA/TCI ideally suited to both military field operations and a wide range of hospital and clinic health care organizations. We expect that TIVA/TCI will eventually become available in the USA, and we believe it is necessary to train a cadre of individuals who are experienced (and “comfortable”) with the basic tenets of TIVA/TCI.

We therefore developed a core of knowledge that clinicians can presently use which will enable them to quickly and seamlessly transition to the full TIVA/TCI systems when they become available.

Methods:

During prior efforts, we analyzed the available TIVA information in multiple articles, web sites and books. We selected only the very essential information needed to enable a practical hands-on learning experience. We developed a set of single page graphics using an intra-venous anesthetic agent simulation program (StanPump.) We added a minimalistic set of text pointing out only the key points. The aim was that each page could be read in 30 – 60 seconds. We produced a set of HTML pages and placed these in an open web site: www.LearningTIVA.com. We encouraged feedback from users to enable us to gauge the perceived value of the site, and make recommendations about future expansion of the site.

The statement of work for the 2009 no-cost extension essentially aimed at:

- Maintaining the web site up and running
- Developing further mechanisms to obtain feedback (using a secure Blog)
- Following up on the PLR (Program Line Review, Long Beach, CA, Jan 2009) committee’s suggestions to apply for funding to approach the FDA for approval of TCI principles. (see page 5 for an explanation of abbreviations)
 - also, requesting larger and longer term funding to greatly expand the web site in the larger context of TeleMedicine and TeleAnesthesia.

Results:

The web site has been available for more than three years. It has been stable, and has not crashed yet. The response has been overwhelmingly positive, with requests for expansion to other TIVA agents.

We had prepared, as an initial effort, a web site that we believed would be suitable for clinicians with some anesthesia experience, e.g. mid-level anesthesia residents. Feedback indicated that even beginner residents (e.g. first night on call), found the web site

extremely useful for a quick just-in-time introduction to the concepts of thinking in terms of achieving constant blood concentrations, in contrast to thinking in terms of constant infusion rates.

For the 2009 no-cost extension, the following RESULTS had been achieved:

- An anonymous (enabling honest feedback) Web Blog was created which enables secure and safe (against hackers) feedback
- The website usage statistics have continuously increased over the period of existence, as an increased number of interested anesthesia care providers have found the site. (The graphic shows the use of the web site for the last few months – see appendix)
- Presentation to the PLR Committee (Jan 2009 Long Beach, CA) with strong support from the committee to continue with further developments of the web site, as well as to approach the FDA for approval of the TCI concept.
- An application for funding was submitted to TATRC in June 2009: this work would expand the web site, as well as fund the approach to the FDA
- An application for a \$4.2 million TeleMedicine Earmark (including TIVA/TGI/TCI) was submitted to the Government Relations Office of Pennsylvania State University College of Medicine for further administrative submission to the Office of Robert Casey (PA Senator).

Discussion:

The application (submitted June 2009) for further funding from TATRC is still under review. The application for the funding for the Earmark was well received by the Office of Government relations of Pennstate.

The web site was designed in 3 sections: a linear learning format, a section on “How to use the simulation programs”, and a just-in-time section which answers clinical questions without having to go through the whole session.

The Blog for feedback has been implemented, and further feedback is being collected and collated.

E.1. Abstract (continued within E. Body)

The web site is in daily use with very positive feedback comments. As expected, the linear section is used the most often, and used most often by more junior personnel. The clinical questions are used by clinicians after very long (3-6 hour) anesthetics, to help them gauge the “time to wake up.” While they found this quite useful, they indicated that it would be even more useful if they could have a “dedicated” program to follow an individual patient with all the exact changes in infusion rates. Therefore, several clinicians indicated that they were interested in using the web site to learn (and practice) how to use the simulation programs to more closely follow their specific clinical case. There were also several requests for more advanced programs to take into account the synergism of agents used simultaneously with one another, and the resulting decrease in blood (plasma) concentrations required to maintain anesthesia and/or sedation.

Conclusions: (of abstract)

The web site has been a huge success, with much positive feedback. We are succeeding in our aim to develop a group of practitioners who are quite familiar and comfortable with thinking in terms of blood concentrations of anesthetic agents.

E. Body (continued)

E.2. Background:

Background to the present project: This is a 3rd extension and follow-on of the project of Phase I (see Appendix 1) which analyzed the requirements of different levels of learners for the pharmacological underpinnings required to understand TIVA/TCI.

We can summarize the requirements of the learner groups as follows:

- juniors were interested in linear learning, i.e. start at the beginning, and sequentially work through the material in a logical sequence.
- more advanced learners were interested in “just-in-time” information. This is also known as asynchronous learning. They wanted to be able to quickly find a single piece of information, answer a single clinical question, without having to wade through a whole slew of information.

The overall goal of the project was to develop a Web Site for a distance education training course (including feedback) in TIVA TCI for military personnel for use at their home base (civilian and/or military) so that they will have the expertise to implement TIVA TCI during their military duties on CONUS as well as in the field hospitals. The need for TIVA has been expressed by all military branches. The anesthesia equipment footprint for TIVA requires much less space. Safety and simplicity are enhanced; there is less maintenance required, and no pollution.

The overall long term project aims to build a cadre of experienced TCI users. These users (civilian and military) will be experienced with TIVA principles whenever the TIVA equipment is deployed.

Background to TIVA in general: Total intravenous anesthesia (TIVA) via target controlled infusion (TCI) use is widespread outside the United States of America. The use of TIVA/TCI in patient care provides excellent anesthesia with minimal over or under-use of anesthetic agents, providing an excellent, safe patient experience and cost effective health care (pharmacy, equipment, and provider team utilization). In addition, compared with other current anesthesia modes, TIVA/TCI equipment is light-weight, easily transported by a single person, and operable without external power. This makes TIVA/TCI ideally suited to both military field operations and a wide range of hospital and clinic health care organizations. We expect that TIVA/TCI will eventually become available in the USA, and we believe it is necessary to train a cadre of individuals who are experienced (and “comfortable”) with the basic tenets of TIVA/TCI.

We therefore developed a core of knowledge that clinicians can presently use which will enable them to quickly and seamlessly transition to the full TIVA/TCI systems when they become available.

Background to web site development: Based on feedback from TATRC on the Final Report submitted by us on Dec 31, 2005, it became clear that TATRC strongly wished us to produce a functioning Web Site for distance learning. Therefore the thrust of this extension is to develop a functional Web Site which would be “open” and accessible from anywhere in the world without any restrictions on access.

Background to steps taken for the project: There were several sequential steps needed prior to building the web site.

- decide on what knowledge to select
 - create the contents of the web site using pharmacological simulation programs
 - develop an overall philosophy for how to present the knowledge (e.g. page length)
 - build the web site, and test all the links and cross referrals (back and forth)
 - open the web site to the world and collect comments for future improvements
- This report describes the process to complete the list as above.

Based on all the background material and initial parts of the project, we then proceeded with development of the web site.

E.3. Task 1: Identify and select information for a web site.

E.3.1. Identified a core of basic, fundamental knowledge for teaching TIVA TCI via the Web.

Based on Phase I of the project, we had a good idea about the content and presentation format for the pharmacological information.

We can summarize the requirements of the learner groups as follows:

- juniors were interested in linear learning, i.e. start at the beginning, and sequentially work through the material in a logical sequence.
- more advanced learners were interested in “just-in-time” information. This is also known as asynchronous learning. They wanted to be able to quickly find a single piece of information, answer a single clinical question, without having to wade through a whole slew of information.

From many years experience of attending lectures and workshops on pharmacology and especially pharmaco-kinetics, we knew that learners were not interested in esoteric information such as exponential wash-outs and tri-exponential fits of data from multiple body compartments. We therefore selected a core of very practical information that we believed would be the minimal essential information needed to adequately understand a different and new way of thinking about TIVA.

We proposed to present a “**new way of thinking about TIVA administration.**” Basically, we suggested that anesthesia practitioners think about establishing a constant blood (plasma) level of the anesthetic agent, using a **decreasing (non-constant) infusion rate**. This is in contrast to the present way of thinking where a constant infusion rate is typically used. This idea was tested in several lectures at different medical institutions (see Reportable outcomes.) Feedback indicated that residents and CRNAs could readily grasp the concept and were willing as well as able to, to implement the concept.

We had selected, as an initial effort, content that we believed would be suitable for clinicians with some anesthesia experience, e.g. mid-level anesthesia residents. (However, feedback indicated that even beginner residents, e.g. first night on call, found the web site extremely useful for a quick just-in-time introduction to the concepts of thinking in terms of achieving constant blood concentrations, in contrast to thinking in terms of constant infusion rates. See below)

E.3.2. Prepared the knowledge base in a curriculum format suitable for implementation in a Web site suitable for teaching TIVA TCI

- We proposed to develop the information in sections that could be read and assimilated in 30 – 60 sec per page. Each page was also designed to fit on a computer screen, so that a user would not need to manipulate the page to see the whole of the contents.
- We designed the content in 3 sections in which to present the information
 - a. a linear learning set of pages which was divided into induction, maintenance and reversal sections
 - a section for advanced users with step-by-step guidance to actually run the simulation program. We produced instructions for 3 commonly used simulation programs (StanPump, StelPump, and TIVATrainer)

E.3.3. Prepared graphics for the web site using a simulation program

Part A: We prepared the graphics for the website by running StanPump to calculate blood concentrations of propofol for typical anesthetic cases. We prepared data for induction, maintenance, and wake-up periods at multiple different infusion rates and durations of anesthesia (from 1 to 12 hours.) We also ran simulations of conscious sedation infusion rates.

We simulated cases of induction of anesthesia using the bolus-excretion-transfer (BET) methodology. This mimics TCI (target controlled infusion) which is typically managed by a computer controlled infusion in Europe. However, this computer controlled infusion technology has not yet been approved by the FDA for use in the USA (and therefore, operator controlled infusion was simulated/prepared for the web site.)

Part B: We wrote detailed instructions for using the simulation programs (StanPump, StelPump, and TIVATrainer.) We wrote only the essential step-by-step instructions needed to perform a common anesthetic, such as a BET induction technique. The programs provide manuals, but the feedback is that the manuals are too detailed, and have too much unnecessary information. Our learners want to immediately start with hands-on learning (e.g. follow instructions), and not have to read through many, many pages of instructions (forgetting many in the meanwhile), and only then starting to actually work with the simulation program.

Part C: We envisaged a whole series of clinical questions that trainees could potentially ask (or have asked in the clinical environment.) For instance:

- how long will my patient take to wake up after an anesthetic of x hours at an infusion rate of y ug/kg/min?
- how many ml of propofol will I need for an anesthetic or conscious sedation of x minutes at an infusion rate of y ug/kg/min?

We also prepared the simulation data to answer such questions.

E.3.4. Constructed each page for the web site with only essential information

The simulation programs provided blood concentrations at 10 sec intervals in a text format (xyz.TXT.) We imported these (often very large) files into an Excel spreadsheet. We rearranged and collated data into graphics files that we could export to a Word program.

We indicated for each graphic what the learning point was for that specific

graphic. That helps the trainee quickly work through each page without having to guess where to look for a specific learning point.

E.3.5. Tested the proposed contents in various teaching and lecture format

The contents were tested in various formats, such as clinical teaching in the OR to all levels of residents and CRNAs, one-on-one teaching in a quiet environment, large lecture format to senior residents and medical students, and Grand Rounds lectures.

E.3.5. Refined the teaching material page-by-page based on feedback

The feedback was used to refine and enhance the content.

E.4. Task 2: Build a web site.

E.4.1. Developed a Web Site with a curriculum to teach TIVA TGI

The web site was designed in 3 sections: a linear learning format, a section on “How to use the simulation programs”, and a just-in-time section which answers clinical questions without having to go through the whole session.

The Word file was decimated to single pages. Each page was converted to HTML format, and renamed in sequential numbered format for ease of insertion into the website. Each page was formatted such that it would fit on the most common small computer screens without the need to use a mouse to find the text on the right hand side of the page.

The HTML format was selected such that the file was left aligned without an actual border on the right hand side. This technique enabled the coloring to sweep throughout the web page, irrespective of the size of the computer screen.

E.4.2. Built the web site as an open web site, accessible from anywhere in the world without restrictions.

A study was made of various places to host the web site. Commercial entities, universities and other institutions were interested in hosting the web site. However, this would mean that the user would have to go through the hosts entry point, which could present problems with firewalls. This would also not enable us to readily update, or add to the web site. Institutions also have their own requirements (colors, font sizes, etc.) to present a uniform web experience to visitors. Hosts would also want to have “ownership” and/or licensing of the web content, and it might not be easy to move the web site to another site when the need arose.

We therefore elected to host the web site as a freestanding entity. We elected to use Yahoo.com as they provided the least amount of potential problems, and a sufficiently open access for anyone to access the web site.

E.5. Task 3: Collect comments and feedback from users of the website

Feedback from users of the web site has been uniformly positive with requests for more details (expanded website), as well as for similar web sites for other medications used during TIVA.

Examples of such comments follow.

E.5.1. Comments from experienced trainees:

The web site was initially designed for anesthesia residents and health care workers with some basis and experience in anesthesia (not necessarily with TIVA.)

Verbal comments from this group (including Senior residents and Nurse Anesthetists (CRNAs) (experienced practitioners) who had done several cases of TIVA before), included:

- Many of these health care workers believed that they did not need a web site, as they had much clinical experience. Typical comments: "I do not need a web site. I have done dozens of TIVA cases." The Attending did not argue with them, but just asked them to look at the first 7 slides on the web site. For instance: "I understand that you have much experience with TIVA. Therefore, please look at the web site, and give me comments on how this web site can be improved for use by juniors and trainees. During the 9 – 12 hours of this TIVA anesthetic, please look at the web site." Invariably, the answers come back:

- "there was so much in the web site that I did not know"

- "there was so much in the web site that I did not understand, before reading it there."

- "I have always used the same infusion rate (just as I always use the same fresh gas flow, and the same setting of the volatile anesthetic agent). I didn't know (understand) that a CONSTANT infusion rate did not provide a constant blood concentration. "

- "I now know that I should think about a constant blood (plasma) concentration."

- "I now know why some patients wake up quickly (short cases.) :I never understood why some patients took so long to wake up. This is now quite clear to me : longer cases take longer to wake up."

- I was always terribly worried during a TIVA case that the patient would become "aware" (awake), and feel (remember) pain. Therefore, I ran excessively high infusion rates, to prevent such events. I disliked TIVA because my patients took so long to wake up. Now I understand that I only need to attain a CP50 (concentration of plasma propofol that will keep 50% of patients from moving during skin incision) of 4 ug/ml for skin incision, and less for non-painful surgery, as well as lower concentrations for skin suture during the ending of the surgery. My patients are now waking up much quicker after a TIVA anesthetic. The surgeons are very happy with my TIVA cases.

- "I now have the confidence to decrease the infusion rate (or even switch off the infusion) long before the end of the case. I can easily check the web site to see how long before the end of the longer cases I can decrease and then discontinue the TIVA agent, as well as be confident and comfortable that the patient will not wake up or be "aware." .

E.5.2 Comments from a variety of personnel included:

Neurosurgeons are also pleased when residents and nurse anesthetists (CRNAs) use principles as explained on the website. The prior high incidence of long, slow awakening (due to running a very high infusions rate right until the end of the case), has decreased markedly. Prior to the web site use, patients could take 1 – 3 hours to wake up after prolonged TIVA cases. The neuro-surgeons were nervous about the slow wake up due to their now knowing if the slow wake up was due to the TIVA, or due to an intracranial bleed. The anesthesia practitioners did not really have any help to indicate the possible wake up period (“context sensitive half-time”), after a given duration of infusion at a given infusion rate. With the help of the web site, such an estimate is now quite feasible. It has now become easy to differentiate TIVA slow awakening from post-operative complications as a cause of the slow awakening. Using the web site with the predictions of the wake up time, relative to the duration of the infusion, the incidence of these very prolonged wake up times have decreased greatly.

Neuro-monitoring technicians are reporting that TIVA cases using the web site principles give them a much more stable platform, so that any changes they observe can be solely attributed to the surgery. They do not have to take widely varying levels of anesthesia depth into account.

The nurses in the **PACU (Post Anesthesia Care Unit)** appreciate TIVA cases as well – much less nausea and vomiting requiring treatment. They also say that the patients are much more clear-headed with a very low incidence of the violent, agitated, uncontrollable patients during the recovery room period. The PACU nurses area asking if we would please use TIVA for all young patients (20 – 40 year old) with a history of alcohol use. They are reportedly much easier to manage, the nurses can talk to them and readily figure out if they have pain, a full bladder, of are having breathing difficulties that could contribute to (or cause) the agitation.

Need for “smooth awakening”: Wake up without coughing and bucking on the endotracheal tube (ETT): using TIVA principles as found on the web site (throughout or towards the end of the anesthetic), is becoming a standard technique to provide a smooth awakening with a minimum of coughing and bucking. The propofol plasma concentration can be gradually decreased (within a context of the duration of prior infusion as per the web site), to the point where the patient is awake and responding to commands, but not coughing and bucking on the breathing tube. This is useful to avoid disruption of sutures, and minimizes the risk of post-operative bleeding. This principle is applicable to a wide range of surgical specialties such as vascular surgery, ENT surgery, orthopedic surgery, facial trauma, major fractures, etc.

Nausea and vomiting prophylaxis: Comments: “I have always known that TIVA caused less nausea and vomiting in the post-operative phase, but I was uncomfortable with using a TIVA based technique. Using the concepts on the web site (attaining a CP50 of 4 ug/ml for skin incision, lower blood concentrations during less surgically stressful periods, etc.), I am know much more willing to use TIVA. I now use it all the time for patients with a strong history of severe post-operative nausea and vomiting. The patients just cannot believe how well they feel after a TIVA technique! I am now getting repeated requests from patients who heard I am willing to use TIVA for patients with a history of nausea and vomiting.”

E.5.3. Repeated use of the web site: (just in time)

Several senior residents reported that they looked at the web site every time before they administered a TIVA. Especially the wake-up sections were found to be of great value. It is not possible to remember all the graphics to match the exact duration of their infusion for that specific patient.

E.5.3. Probably the most telling comments from the residents were that they now thought totally differently about TIVA (i.e. they said that they had developed a new approach): instead of thinking about a single “best” or “ideal” infusion rate, they were now thinking about an adequate blood concentration and adequate blood level of propofol.

- they understood (internalized) that the required blood level varied for various phases of the surgery: e.g. a high level for induction, intubation, dissection, etc., and a lower level for closure and skin suturing.
- They understood the need to decrease the blood level/concentration towards the end of the anesthetic to minimize the wake up time (they believed they really understood context sensitive half times, and could apply the knowledge to their patients.)

E.5.4. Comments from juniors and beginners:

Junior resident (inexperienced in TIVA practitioner)

- Experience with, and comments from a new junior resident – first night on call (after 3 months of Operating Room training, and 3 months of general internship after medical school). A patient for emergency neuro-surgery required neuro-monitoring, which necessitated TIVA (total intra-venous anesthesia). While the resident was very comfortable with the prior emergency patients requiring general anesthesia with volatile agents (such as isoflurane, sevoflurane, or desflurane), the resident was extremely uncomfortable (read “scared”) with the concept of giving a TIVA anesthetic, as this would be the very first case of TIVA. The resident had never done a TIVA case, nor seen a TIVA case. The attending suggested that the resident read the first 7 slides (30 – 45 seconds per slide to read and understand) on the web site (www.LearningTIVA.com), while the attending set up the anesthetic work station in the operating room. After reading the first 7 slides, the resident said: “I am very comfortable. I can do this. I now understand what I need to do to obtain a constant blood level of propofol. This is an excellent web site, I can work with this.” As this was quite a long case, the resident also had time to read more of the web site and had a very good idea of the wake up process.

Mid level resident (some prior experience with TIVA)

- Mid level residents who had some prior experience with TIVA, reported that they were still uncomfortable with TIVA. While they could “manage” the case, they reported that they did not really understand what they were trying to achieve. For instance, they would say: “I have done several TIVA cases. I followed the instructions for a given infusion rate. It worked for me.” After following a suggestion to read the first 7 slides on the web site, they typically would say: “This web site is great! I now know what I was supposed to do. This now makes sense. I did not really know what I needed to do, prior to reading the web site. I wish someone had shown this to me before. I would have gained much more value from my clinical experience.”

E.5.6. Medical Students:

- While the web site was not developed with the very beginner anesthesia practitioner in mind, medical students who have looked at the web site have uniformly reported that they found much value in understanding the principles of infusion, after reading the web site. They reported that the principle of giving only the main points on each graphic, and specifically pointing out exactly what was the lesson on each page, was a very efficient way of learning. They asked for more such web sites, specifically informing about complex concepts such as pharmaco-kinetics.

E.5.7 Comment about web site from a Nurse Anesthetist (CRNA) after a Grand Rounds that included a significant section on the contents of the website

We used the TIVA principles you described, and it worked well for us (CRNA and Student CRNA – SRNA)

E.5.8. Suggestions by trainees for future use and expansion:

Most trainees said they thought it would be a good idea to have a computer program to simulate their specific patient (i.e. TGI – target guided anesthesia), so that they would have an even better idea of what the blood concentrations were at any given stage, and also how long it would be to “wake up time” (i.e. how soon to switch off the anesthetic infusion.)

They also mentioned that it would be difficult for an individual to keep all the blood levels/concentrations and wake up times in memory when multiple agents would be used simultaneously. Specifically, dexmedetomidine and ketamine are now becoming regular additions to propofol, fentanyl and muscle relaxants. Therefore, they would like to see an expanded web site as an interim step (until computer programs become available.)

E.5.9. Concluding comment about comments on web site:

The web site is in daily use with very positive feedback comments. As expected, the linear section is used the most often, and most often by more junior personnel. The clinical questions are used by clinicians after very long (3-6 hour) anesthetics, to help them gauge the “time to wake up.” While they found this quite useful, they indicated that it would be even more useful if they could have a “dedicated” program to follow an individual patient with all the exact changes in infusion rates. Therefore, several clinicians indicated that they were interested in using the web site to learn (and practice) how to use the simulation programs to more closely follow their specific clinical case.

Conclusion (Body)

The purpose of the project was to create a website to promote the learning of TIVA, and enable development of a cadre of clinicians experienced and comfortable with TIVA. The open website that was developed consists of a minimum body of knowledge that can rapidly be accessed from anywhere in the world. Each page can be read in 30 – 60 seconds. User feedback indicates that this website (www.LearningTIVA.com) is a great success and succeeding in its purpose.

F. Key research accomplishments

Bulleted list of key research accomplishments emanating from this research

Summary of tasks performed:

- **Identified** a core of basic, fundamental knowledge for clinically relevant teaching of TIVA TCI concepts via the Web.
- **Prepared** the knowledge base in a curriculum format suitable for implementation in a Web site suitable for teaching TIVA TCI
- **Prepared graphics** for the web site using a pharmaco-kinetic simulation program
- **Constructed** each page for the web site with only essential information – each page can readily be read in 30-60 seconds
- **Tested** the proposed contents in a lecture format
- **Refined** the teaching material (page-by-page) based on feedback
- **Developed a Web Site** with a curriculum to teach TIVA TGI
- **Built** the web site as an open web site, accessible from anywhere in the world without restrictions
- **Maintained** the website for three years in a fully functional state
- **Collected** further verbal comments from users of the website
- **Created** an accompanying Web Blog site for safe and secure feedback
- **Built links** into the web site to the Web Blog
- **Applied** for further funding (as per PLR suggestions): TATRC and an earmark through Penn State College of Medicine

Please see “Body” for a detailed description of each of these steps

Please see the “Introduction” page for explanations of abbreviations and terms.

G. Reportable Outcomes

- **Built an open web site – open to any user, anywhere in the world.**
www.LearningTIVA.com
- Built an accompanying web Blog site
www.LearningTIVA.Blogspot.com
- Funding application (June 2009) for expanding the work and approaching the FDA (as per suggestions by the PLR committee, Long Beach, CA, Jan 2009)
- Funding application 2009-2010 : for an Earmark (\$4.2 million) through Penn State College of Medicine, Government Relations Office
- Murray WB, Fortner M, Rosenwasser E, Gordin G. Understanding Relationships between Infusion Rates and Plasma Concentrations Improves Safety of TIVA Anesthesiology 2006: 103 (abstract published on CD of proceedings)
- Abstract and poster presentation competitively selected for the Annual Conference of the American Society of Anesthesiologists, ASA Meeting, Chicago. Il, Oct 2006 Murray WB, Fortner M, Rosenwasser E, Gordin G. Understanding Relationships between Infusion Rates and Plasma Concentrations Improves Safety of TIVA, The Pennsylvania State University College of Medicine
- Abstract and poster presentation competitively selected for the Annual Conference of the American Society of Anesthesiologists, October, 2005, New Orleans, LA: Title: Target Guided Infusion (TGI): using technology to improve understanding of pharmacokinetic and pharmacodynamic principles. W. Bosseau Murray, Benjamin H. Boedeker, Robert Marine, Celestine Okwuone, The Pennsylvania State University College of Medicine, University of Nebraska Medical Center/Omaha VA Medical Center, and Telemedicine and Advanced Technology Research Command (TATRC), Fort Detrick, MD. (see Part I)
- The idea underlying the web site, i.e. thinking about obtaining a constant blood (plasma) concentration, was tested in Grand Rounds and other lectures at several institutions. The web site was advertised at these lectures. Informal feedback and comments were requested.

Boston Medical College: Grand Rounds August 7, 2005 (based on the Anesthesiology Newsletter article Oct 2005 and also their interest in computer controlled anesthesia delivery) Title of the talk: The Future of Anesthesia Delivery (including TIVA/TGI).

Omaha, Nebraska Dec 2005 Grand Rounds Joint with Nebraska VA Medical Center: The Future of Anesthesia (including TIVA-TGI)

Penn State University Core lecture Senior Anesthesia Residents Dec 2005– Anesthesia for Geriatrics (including TIVA-TGI for Geriatrics and poor risk patients)

Society for Education in Anesthesiology (SEA) Fall Meeting, Chicago, IL Oct 2006
SEA/Duke Award for National Meritorious Service to Anesthesia: Acceptance speech
Murray WB Unexpected Beneficial Effects of Interdisciplinary Simulation at a Systems Based Practice Level (including aspect of TIVA working with pharmacologists)

PennState University Dean's Invited Lecture Nov 2006 by Murray WB
The future of medical education and virtual reality (including TIVA)

Joint Cornell University Medical Center and Memorial Sloan Kettering Cancer Center
Visiting Professor Anesthesiology Grand Rounds Conference on March 19, 2007
Title: Future of Anesthesia delivery systems (including TIVA – TGI)

Scott and White, Temple, Tx, Resident Research Day March 2007, Invited Guest
Speaker: The Future of Anesthesia aspects of delivery and monitoring (including TIVA-TGI)

PSU Core lecture junior students October 2007: Intra-venous Anesthesia Induction Agents (including TIVA – TGI)

- The idea of using TIVA formed the subject of two medical student research projects (in parallel with the TATRC project.) The concept of teaching and learning TIVA, using pre-printed graphics with minimalistic information per page (i.e. only the essential information), was highly valued by the academic community, and both MSR projects were awarded a prize and selected for presentation at the MSR award ceremony.

Medical Student Research Symposium, PennState, April 27, 2006
Michael C. Fortner MSIV, Murray WB
Selected for poster presentation at MSR award ceremony

Developing a Curriculum: Understanding and Applying Pharmacokinetics to Improve Safety and Efficacy During Infusions of Medications
Fortner M, Murray WB, 2006, Medical Student Research Project
TIVA Curriculum using simulated pharmaco-kinetics

Nace M, Murray WB Medical Student Research (MSR) Project 2007
Clinicians' perceptions of the educational value of a graphic printout as a guideline during TIVA (total intravenous anesthesia)

Medical Student Research Symposium, PennState, April, 2007

Nace M , Murray WB

Clinicians' perceptions of the educational value of a graphic printout as a guideline during TIVA (total intravenous anesthesia)

Selected for poster presentation at PennState University MSR award ceremony

Grand Rounds, Department of Anesthesiology, Pennsylvania State University College of Medicine, Sept 2008

“The Future of Anesthesia” which included a significant section on TIVA with promotion of the website.

Murray WB, Vaduva S, Berg BW

TeleMedicine, TeleAnesthesia and TeleSurgery

Book Chapter in Urmann (Ed) Associated site Anesthesia 2009

Research Opportunities:

Further Medical Student Research Projects developing graphics based on pharmacokinetics of more agents for inclusion into the web site (www.LearningTIVA.com)

H. CONCLUSION:

Summarize the results to include the importance and/or implications of the completed research and when necessary, recommend changes on future work to better address the problem. A "so what section" which evaluates the knowledge as a scientific or medical product shall also be included in the conclusion of the report.

Phase I of the research had produced information critical to creating viable education system structures, curriculum elements (lessons, sessions, modules, and adjunct resources), resources for distributed delivery of meaningful, equivalent, and learner transportable, education throughout the military and civilian anesthesiology provider groups.

In the Phase II no-cost extensions, we developed and provided a web site (www.LearningTIVA.com) to teach TIVA principles to anesthesia residents and other administering propofol in and out of the OR (e.g. CRNAs and conscious sedation nurses) The information was carefully selected to be the minimum needed to provide understanding ("get the message across") of a new way of thinking of blood concentrations.

Based on results from an earlier project funded by TATRC, the information was presented as a linear learning sequence (for beginners and novices), as well as a just-in-time series of clinical questions (for more experienced personnel.)

The feedback indicated that trainees could use the web site and readily/quickly, not only grasp the new concepts, but also apply the new concepts in the clinical arena.

The trainees suggested future expansion of the work to include:

- a dedicated simulation program to give more detail and granularity of their specific patient (TGI principles – target controlled anesthesia - see "Introduction page for an explanation of abbreviations and concepts)
- more medications to be included in the web site.

Importance:

The importance of the project was stressed by the members of the PLR (Program Line Review, Long Beach, CA Jan 2009): they indicated that there was a great need for a simplified anesthesia administration system, such as TIVA-TCI, with a much smaller footprint than the anesthesia machine or a draw-over vaporizer. The system should be approvable by the FDA for use in the USA (e.g. civilian use for anesthesia practitioners pre-deployment.)

Implications;

The development of appropriate TIVA training material:

- improves the safety for the war fighter undergoing anesthesia and sedation due to a better understanding and application of TIVA techniques
- increases the likelihood that the anesthesia practitioner will use the safer and simpler TIVA technique

Military Relevance of TIVA TCI education:

Here we discuss the “**so what**” relevance of this project.

- i. Increased number of surgical patients treated in both forward-deployed and out-of-theater medical facilities.
- ii. Increased efficiency of the health care delivery system through effective delegation of responsibilities for surgical patients requiring anesthesia care.
- iii. Initial development of medical education system, including simulation, which is distributed from a central location.
- iv. Initial development of medical education system, including simulation, that is transportable with the learner with reassignment.

The potential military relevance of this protocol is that we could accomplish the vision of educating a group of anesthesia practitioners in the use of a portable TCI system for battlefield use which would have significantly less weight and cube than presently used volatile agent anesthesia systems.

Prior to the proposal of this protocol, attempts were being investigated in the DOD studying TCI devices which are approved in Europe but not in the US. These cannot be fielded for military use without obtaining a 510K which has to date proven to be unattainable. Our approach will guarantee a win in this arena as we start developing a group of experienced users of TIVA TCI. This will be an excellent first step to field TCI capability to the DOD as we march toward full approval of the TCI systems.

The proposed implementation also allows a significantly large group of providers to engage in an experiential learning opportunity under guidance in the military and civilian operating theaters. This project will be developed in further phases to produce a well-constructed educationally sound offering. This education mode, if determined to be useful to these providers, might be a form of education that is easily integrated in the field, providing education simultaneously with ongoing patient care: saving time and lives.

Safety is also enhanced as the TIVA equipment is much less complex (less to go wrong) than anesthesia machines employing volatile agents.

When volatile agents are not used, any ventilator can be used as there is no need for re-circulation of expensive and polluting gases (nitrous oxide) and volatile anesthetic agents (isoflurane, sevoflurane and desflurane)

There is also no need for complex and/or low flow breathing systems as no pollution is occurring. Scavenging systems for polluting volatile agents and nitrous oxide are also not required.

Significance of the Effort

The significance of this effort lies in both added health care capability and preliminary experience and education for a target group of anesthesia health care providers.

Our protocol will allow a venue to train users at the present time in the concepts of a target controlled infusion (TCI) device which will eventually be fielded by the military in a manner that will be FDA approved.

This will accomplish a major developmental objective identified by the anesthesia consultants from all three medical services.

When the full TCI device is eventually approved by the FDA, there will then already be a significant community of educated users of TCI that could rapidly implement the system in the military units.

The significance of the TIVA devices also includes:

- The smaller footprint of TIVA devices
- Less weight
- Less complex equipment
- Less maintenance
- No noxious fumes and no pollution from volatile agents (that need to be scavenged and disposed)
- Less complex ventilator (just about any ventilator will do – not necessary to be compatible with administration of volatile anesthetic agents)
- Less need for a ventilator (more spontaneous ventilation = less muscle relaxants = safer)
- no need for a specific anesthesia breathing system nor for soda lime to absorb carbon dioxide)
- a single system that could be used pre-, intra-, and post operatively = fewer changing of connections and re-connections, less chance for error, = safer
- enhanced safety due to much simplified equipment, and much simpler use

Uniqueness: there is no other method or effort underway to develop a large group of experienced anesthesia practitioners in TIVA TCI skills in the military.

Recommended changes and future work:

So what? Where do we go from here? Multiple very valuable ideas were suggested during the feedback phase. For instance:

- There were several requests for more advanced programs to take into account the synergism of agents used simultaneously with one another, and the resulting decrease in blood (plasma) concentrations required to maintain anesthesia and/or sedation
- Clinical trials involving learners were suggested at military and non-military institutions using the latest TIVA infusion pumps. This could take the form of a backbench study, i.e. using a simulation program to advise the user as one of a multitude of points of information on when to adjust the infusion rates.
- a dedicated simulation program to give more detail and granularity of their specific patient (TGI principles – target controlled anesthesia - see “Introduction page for an explanation of abbreviations and concepts)
- more medications to be included in the basic web site.
- the website www.LearningTIVA.com is deemed by users to be of great value in increasing their understanding as well as their comfort level of using the TIVA techniques, and therefore, increases the likelihood that the simpler and safer TIVA technique will be selected and employed.

- **The PLR committee strongly recommended** that the FDA be approached to approve techniques and/or equipment (widely used in Europe) that could administer TIVA in the form of TCI (target controlled anesthesia, where the infusion rate is computer controlled to maintain a constant blood/plasma level of the anesthetic agent.)

Final summary and conclusion:

The overall goal of the project was to develop a Web Site for a distance education training course (including feedback) in TIVA TCI for military personnel for use at their home base (civilian and/or military) so that they will have the expertise to implement TIVA TCI during their military duties on CONUS as well as in the field hospitals.

This is part of an overall long term project which aims to build a cadre of experienced TCI users. These users (civilian and military) will be experienced with TIVA principles whenever the TIVA equipment is FDA approved and needs to be deployed.

This web site is an essential first step in the direction of introducing TIVA/TCI to a wider USA military and non-military audience.

The PLR committee strongly recommended that the FDA be approached to approve techniques and/or equipment (widely used in Europe) that could administer TIVA in the form of TCI (target controlled anesthesia, where the infusion rate is computer controlled to maintain a constant blood/plasma level of the anesthetic agent.)

I. References

1. Russell D, Wilkes MP, Hunter SC, Glen JP, Hutton P, Kenny GNC Manual compared with target-controlled infusion of propofol
Br J Anaesth 1995; 75: 562 - 566.
2. Servin F TCI compared with a manually controlled infusion of propofol: a multi-centre study Anaesthesia 1998; 53 (Suppl 1): 82 - 86.
3. Struys M, Versichelen L, Thas O, Herregods L, Rolly G Comparison of computer-controlled administration of propofol with two manually controlled techniques Anesthesia 1997; 52: 41 - 50.
4. Bailey JM, A technique for approximately maintaining constant plasma levels of intravenous drugs, Anesthesiology 1993; 78: 116 - 123.
5. Martin DE, Clapin AO, Murray WB, Boedeker BH, 10th Annual SAMBA Meeting, April 1995, Effects of drug synergism and target controlled administration on dose of propofol required to induce anesthesia in adult outpatients.
6. Murray, W. B. Implementation of target controlled anesthesia and analgesia in the austere situation and far forward front. Invited lecture at the 10th Annual Trauma Anesthesia and Critical Care (ITACCS) Symposium 1997, Baltimore, MD (May 15-17, 1997)
7. Murray, W.B. Military uses of target controlled anesthesia. Invited Lecture to the Students, Faculty and Staff of the US Uniformed Health Sciences University 1995, Washington, DC, (January 1995).
8. Marine, R. J. A systems framework for evaluation of faculty Web-work. In C. L. Colbeck, (Ed.), Evaluating faculty performance. New Directions for Institutional Research 2002, no. 114. San Francisco: Jossey-Bass.
9. Colbeck, C. L., Cabrera, A. F., & Marine, R. J. Faculty motivation to use alternative teaching methods. Paper presented at the annual meeting of the American Educational Research Association 2002, April, New Orleans, LA.
10. Murray WB, Fortner M, Rosenwasser E, Gordin G. Understanding Relationships between Infusion Rates and Plasma Concentrations Improves Safety of TIVA Anesthesiology 2006: 103 (abstract published on CD of ASA proceedings)
11. Murray WB The future of anesthesia delivery: from art-based science to science-based art American Society of Anesthesiologists Newsletter 2004; 68(10):7-8
12. Murray WB, Vaduva S, Berg BW
TeleMedicine, TeleAnesthesia and TeleSurgery
Book Chapter in Urmann (Ed) Associated site Anesthesia 2009

Web pages and URLs.

13. EuroSIVA Society European Society of Intra-venous Anaesthesia,
www.eurosiva.org/
14. Web site funded by TATRC to teach TIVA-TCI-TGI
www.LearningTIVA.com
15. Web Blog for feedback on the TIVA web site
www.LearningTIVA.blogspot.com

J. Appendix.

Appendix 1: Information relating to the prior project

This is an extension to the Protocol

"Provider Needs for Distributed Simulation Education System in Total Intravenous Anesthesia & Target Controlled Infusion",
submitted by WB Murray MD as the PI and Professor Robert J. Marine as the Co-PI,
College of Medicine, Department of Anesthesiology, Penn State College of Medicine,
Penn State University, Hershey, PA;

Proposal 04054021, Award Contract No. W81XWH-05-1-0321, HSRRB Log A-13325

The final report was submitted December 2005.

A report was also submitted 30 November 2007 after the no-cost extension

Appendix 2: Personnel funded from the TATRC grant:

No personnel were funded by the grant for the period of the no-cost extension (2008 – 2009)

J. Appendix. (continued)

Appendix 3: Screen capture of example page from a narrow screen

Notice how the text “wrapped” and the graphics automatically shifted (moved) to the left to (compared to Appendix 5) enable the screen to be viewed without the need to use the mouse (cursor) to make the right hand side of the graphic visible.

[Home](#) [Restart](#) [Glossary](#) [Contact](#)

[Back](#) [Forward](#)

Module A
BET
Bolus, Excretion, Transfer Concepts

B.E.T. allows for rapid induction of general anesthesia, (quickly attaining CP50) while maintaining safe blood plasma concentrations.

The doses that are currently accepted begin with

- a 2.5 mg/kg initial bolus, directly followed by
- an infusion of 200 ug/kg/min for ten minutes, then
- 166 ug/kg/min for ten minutes followed by
- 133 ug/kg/min until the end of the procedure.

(Note that different units are used in Europe: 12, 10, and 8 mg/kg/hr.)

70 kg Male D.C.T.

Time (min)	Plasma Concentration (ug/ml)
0	0
5	7.8
10	5.5
20	4.0
30	3.8
40	3.6
50	3.5
60	3.5

J. Appendix. (continued)

Appendix 4: Screen capture of example page from a wide screen

Notice how the page automatically expanded to the right hand side to completely fill the screen. The graphic also moved to remain in the middle of the page.

On a large screen, the page would be seen with a much larger font than this graphic which was formatted to fit into a standard page width.

Home Restart Glossary Contact

Back Forward

Module A
BET
Bohus, Excretion, Transfer Concepts

B.E.T. allows for rapid induction of general anesthesia, (quickly attaining CP50) while maintaining safe blood plasma concentrations.

The doses that are currently accepted begin with

- a 2.5 mg/kg initial bohus, directly followed by
- an infusion of 200 ug/kg/min for ten minutes, then
- 166 ug/kg/min for ten minutes followed by
- 133 ug/kg/min until the end of the procedure.

(Note that different units are used in Europe: 12, 10, and 8 mg/kg/hr.)

70 kg Male O.C.T.

Time (min)	Plasma Concentration (ug/ml)
0	0
5	7.5
10	3.5
20	2.5
30	2.0
40	1.8
50	1.6
60	1.5

J. Appendix. (continued)

Appendix 4:

Monthly usage of the web site www.LearningTIVA.com
September 2009 - February 2010

Note: there are about 400 – 600 users per month

